Auditory Localization as Revealed by

Functional Magnetic Resonance Imaging

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By

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Dedication

I would like to thank my family and friends for all of their support over the years. Without it I don't think I'd be here today. They knew I could do it even when I didn't. They helped keep me motivated and on track. For that I am eternally grateful. Thank you all so much.

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Abstract

Auditory Localization as Revealed by
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Jessica Marie Matthes
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The purpose of this study was to investigate the role of the parietal lobe in auditory localization through functional magnetic resonance imaging (fMRI). Previous cortical lesion research as well as research conducted with positron emission topography suggests that the parietal lobe is involved in the ability to localize the direction of a sound source. The right parietal lobe may play a particularly important role. Nine participants, wearing headset microphones that hung down within the auditory canal, sat on a chair in the middle of a room. Sound recordings were taken from eight different locations around them (0°, 45°, 90°, 135°, 180°, 225°, 270°, & 315°). These recordings were played back for the participants through a set of headphones while in the MRI scanner and participants were instructed to try to determine the location of the sound. Results revealed bilateral activation of the temporal, frontal, and parietal lobes. A region of interest analysis of the parietal lobes revealed that the right hemisphere was not significantly more active than the left parietal lobe during the localization task. This finding was inconsistent with the hypothesis that

significantly more activation in the right parietal lobe would occur during auditory localization tasks.

1. GENERAL INTRODUCTION

It is auditory localization that provides us with the ability to determine the location of the source of a sound in space. This can be done with or without corresponding visual input. Unlike vision in which information about location is projected directly on to the retina, auditory localization involves taking predominately binaural cues and transforming that information into exogenous spatial positions. Information needed for the auditory system to accurately localize sounds includes the difference in time it takes a sound wave to reach each ear, the difference in the intensity of the sound wave at each ear, and the filtering of sound waves by the external ear.

Much of the information about localization is sorted at the lower levels of the central nervous system. For example, the cochlear nerve transmits information about the frequency of a sound stimulus. The superior olivary complex then processes information based on frequencies to provide information about differences in the time and intensity of the sound waves reaching each ear (Pinek, Duhamel, Cave, & Brouchon, 1989). However, it appears that localization is not possible without the involvement of higher cortical functions.

Cortical lesions studies have shown that specific regions of the cortex are necessary for accurate sound localization. (Pinek, Duhamel, Cave, & Brouchon, 1989; Sanchez-Longo & Forster, 1958). For example, lesion studies have shown

that the primary auditory cortex of both primates and cats is involved in auditory localization (Heffner & Masterson, 1975; Cranford, Ravizza, Diamond, & Whitfield, 1971). Studies involving humans with left and right hemisphere brain damage have shown the same effect (Haeske, Canavan, & Homberg, 1996).

While the primary auditory cortex plays a role in auditory localization it appears the parietal lobe plays a particularly important role. Studies have shown that participants with parietal lobe damage have difficulty localizing sounds, particularly when the damage is in the right parietal lobe (Pavani, Ladavas, & Driver, 2001; Pinek, Duhamel, Cave, & Brouchon, 1989). In addition, imaging studies have shown significant levels of activation of the parietal lobes during auditory localization tasks (Zatorre, Bouffard, Ahad, & Belin, 2002; Weeks et al., 2000; Bushara et al., 1999).

1.1 Basic Physics of Sound

Sound results from the oscillation of air molecules. Movement of objects in the environment produces fluctuations in the surrounding air and some of these small changes in pressure are detected by the hearing apparatus as a sound wave. Regular oscillations of the pressure wave produce the perception of a pure tone; complex fluctuations of the pressure wave are perceived as a complex sound. (Moore, 1992). As a sound wave travels from its source to the ear it

becomes weaker. The sound wave is also reflected and refracted off of objects. As a result, what the ear perceives differs from what was originally generated (Goldstein, 2002).

From both a physical and mathematical perspective the sine wave, also called the sinusoid, is one of the simplest types of sound wave. The tones produced from sine waves are pure and are referred to as simple or pure tones. The three key features of a sound wave are its frequency, amplitude, and phase. Frequency refers to the number of times per second a sine wave repeats its self. The frequency of a sound is measured in hertz (Hz) where one Hz is equivalent to one cycle per second. Amplitude is the amount of pressure variation and the phase of a sound wave refers to the number of cycles the wave has completed as measured from a fixed point in time (Moore, 1992).

1.2 Anatomy of Hearing

The ear is composed of three distinct parts: the outer ear, the middle ear, and the inner ear. The job of these three components is to deliver an auditory stimulus to its receptors, translate the sound wave into an electrical signal and finally process the electrical signal to provide information about frequency, volume and sound location (Goldstein, 2002; Martin, 1996).

The outer ear is composed of the pinna, the auditory canal and the tympanic membrane. Pinnae, what most people think of when they hear the word "ears," are the structures attached externally to both sides of the head. The pinnae's main functions are to help localize sound. The shapes of the pinnae are unique to each person. There is no correlation between the shape of a person's pinnae and their ability to accurately localize sound. How an individual's pinnae filters sound is unique to that person. The unique characteristics of an individual's pinnae can be linked to differences in the ability to accurately localize sound that have not been filtered by that individual's pinnae first. For example, if an individual hears a recorded sound played through a set of headphones that was not first filtered by their pinnae they will have difficulty localizing where the sound originated (King, Schnupp, & Doubell, 2001; Wrightman & Kistler, 1993).

As a sound wave approaches the ear it first passes by the pinna and enters the auditory canal, which is approximately three centimeters (cm) long. The purpose of the auditory canal is to help enhance the intensity of sound through resonance. It also serves to protect the tympanic membrane (more commonly referred to as the eardrum), which is located at the end of the auditory canal. Resonance occurs when a sound wave travels down the auditory canal and is reflected back off the tympanic membrane. The reflected sound wave then

interacts with new incoming sound waves. The interaction between the reflected and the new sound waves serves to reinforce a sounds frequency (Goldstein, 2002).

As a sound wave reaches the end of the auditory canal it causes the tympanic membrane to vibrate. This vibration is then translated to the ossicles – the structures that compose the middle ear. The ossicles are made up of the three smallest bones in the human body: the malleus, the incus and the stapes. The vibration of the tympanic membrane causes the malleus, to which it is directly attached, to vibrate. The malleus passes vibrations on to the incus, which in turn passes vibrations along to the stapes. The stapes then passes vibrations to the oval window, which is the opening between the middle and inner ear.

The purpose of the middle ear is to aide in the transmission of an air borne sound wave to the fluid filled inner ear, as low-density airwaves are not transmitted well to high-density liquids. The ossicles help transmit the airwaves to the inner ear in one of two ways. First, they concentrate the vibrations of the relatively large tympanic membrane onto the much smaller footplates of the stapes, which are in direct contact with the oval window. Second, the malleus and incus are hinged and act like an Archimedes lever (Goldstein, 2002). These two strategies combine to create enough pressure on the oval window to move the fluid located in the spirally coiled cochlea of the inner ear.

The cochlea is made up of three fluid filled canals. Within the middle canal lays the organ of Corti, a structure that contains the auditory receptors. The organ of Corti rests on the basilar membrane and is covered by the tectorial membrane. Within the organ of Corti are two layers of hair cells: the inner hair cells, arranged in a single row, and the outer hair cells, arranged in three or four rows. The cilia of the hair cells move or bend as a result of pressure changes in the fluid of the cochlea caused by the movement of the stapes on the oval window. As the cilia bend they brush against the overlying tectorial membrane. This action enhances the response of the hair cells.

Different locations on the basilar membrane respond to specific sound frequencies. High frequency sound waves cause the hair cells near the base of the cochlea to move, whereas low frequency sound waves affect hair cells near the apex of the cochlea. As the cilia of a hair cell bends in one direction it depolarizes the cell and when bent in the opposite direction the cell hyperpolarizes. This pattern of activity causes a burst of firing that passes information about the frequency of a sound stimulus to the auditory nerve fibers (Goldstein, 202). As the auditory nerve fibers from each hair cell emerge from the organ of Corti they form the cochlear nerve portion of the vestibulo-cochlear (VIII cranial) nerve.

1.3 Auditory Pathway

Axons in the cochlear nerve portion of the VIII cranial nerve terminate in the ventral and dorsal cochlear nuclei located in the medulla. The cochlear nucleus neurons then project rostrally into the pons. While many axon fibers decussate forming the trapaziod body some fibers remain ipsilateral. Some cochlear inputs terminate bilaterally in the superior olivary complex while other inputs project to the lateral leminscus and then terminate in the inferior colliculus (Martin, 1996).

While most fibers of the lateral leminscus terminate upon reaching the inferior colliculus some fibers continue past the inferior colliculus and extend to either the dorsal or ventral medial geniculate bodies via the brachium of the inferior colliculus. Fibers from the ventral geniculate body then project to the primary auditory cortex (Brodmann's area 41). Dorsal geniculate body fibers extend to the secondary auditory cortex (Brodmann's areas 42 and 22) (Martin, 1996).

The same tonotopic organization found within the organ of Corti is apparent in the primary auditory cortex such that low frequencies are represented rostrally and high frequencies are represented more posteriorly and medially (Wessinger, Buonocore, Kussmaul & Mangun, 1997). While the

primary auditory cortex is located in the temporal lobe, secondary auditory regions extend into the parietal lobe (Rosenblatt, 1999).

1.4 Auditory Localization

Unlike vision, in which information about an object's location is projected directly onto the visual receptors, auditory stimuli provide information about volume and frequency only. There is no direct reference to the sound location contained in the stimulus. As such, the auditory system has to incorporate information about how sound stimuli interact with the head and ears to determine the location of sound. According to the Duplex Theory of Localization the auditory system accomplishes this in two ways: intraaural time differences and intraaural intensity differences (Rosenblatt, 1999; Wrightman & Kistler, 1993; Yost, Popper & Fay, 1993).

The difference in time it takes a sound to reach one ear before the other is referred to as the intraaural time difference (ITD). For example, if a sound source is located to the right of a listener the sound wave will reach the right ear before the left ear. The delay in time a sound takes to reach both ears can be used as a cue to the azimuth (horizontal coordinate) of a sound source. The only instance in which a time delay does not occur is when a sound originates directly in front of a listener (azimuth of 0°). In that case the sound wave would reach both ears

at the same time and have an ITD of zero. As a sound source is moved to the side of the listener, such that it is directly opposite one of the ears, the ITD increase to a maximum of 600 microseconds (Middlebrooks & Green, 1991). A number of studies have shown that humans can detect ITDs as little as 10 microseconds (Durlach & Colburn, 1978; Kind, Schnupp, & Doubell, 2001). ITDs are most prominent when a sound is of a low frequency (Martin, 1996).

The other cue the auditory system uses to determine the location of a sound source is the intraaural level difference (ILD), which is the difference in the level of the sound pressure reaching the two ears. The ILD occurs as a result of the acoustic shadow a listener's head creates as a sound wave passes by. The ILD is a function of the wavelength of sounds. Shorter wavelengths associated with high frequency sounds are more easily disrupted by the size and shape of a listener's head and, as such, create a greater difference in the sound pressure intensity at each ear (Middlebrooks & Green, 1991). The longer wavelengths associated with low frequency sounds are relatively unaffected by the dimensions of a listeners head, therefore the sound pressure level reaching the two ears is of equal value.

Information about ITD and ILD are sent via the anteroventral cochlear nucleus to the superior olivary complex where they are initially processed. The medial superior olivary complex is sensitive to ITDs as they respond selectively

to low-frequency tones. The lateral superior olivary complex, which is more sensitive to high frequency tones, processes information about ILDs (Martin, 1996).

Intraaural time and level differences are well suited to provide information about the location of a sound source when it is in the horizontal plane however they offer little information about the elevation of a sound source. For example, if a sound source is located directly in front of a listener at any elevation the ITD and ILD are zero as the sound waves travel exactly the same distance to both ears (Goldstein, 2002). Therefore, some other information is needed to aid the listener in determining the elevation of a sound source. Cues about elevation are provided by spectral cues and are related to how the head and pinnae affect the frequencies of sound stimuli.

As a sound source approaches the listener's head it is first reflected from the head and reflected within the various folds that make up an individual listener's pinnae. A study by Gardner and Gardner (1973) revealed just how crucial the role of the pinnae are in localizing sound. By inserting modeling compound into the folds of a listener's pinnae thereby making it a smooth surface they demonstrated that it was more difficult for a listener to localize the direction of a sound source.

The reflections of sound waves off of the head and within the folds of the pinnae affects the frequency of the sound, such that the sound entering the auditory canal is of a different frequency than when originally produced from the sound source. The difference in frequency from when a sound is initially emitted from a source to when it enters the auditory canal is known as the head-related transfer function (HRTF) (Middlebrooks & Green, 1991; Wrightman & Kistler, 1993). The way in which a sound wave interacts with the head and the folds of the pinnae causes an increase in the intensity of some frequencies, while decreasing the intensity of other frequencies. For example, a study by Middlebrooks (2000) revealed there is a decrease in the HRTF at 6,000 Hz, 11,000 Hz, and 14,000 Hz. If a sound wave approaches a listener directly from the front there is a decrease at 10,000 Hz but an increase at 13,000 Hz. When a sound wave approaches from overhead, a decrease in the HRTF occurs between 8,000 Hz and 10,000 Hz.

The distance of a sound source to the listener also affects the listener's ability to judge location. In general, it is easier to judge distance the closer the sound source is and distances within an arms length are the easiest to judge. Research suggests that listeners tend to underestimate the distance of a sound source when it is more than an arm's length away (Loomis, Klatzky, & Golledge, 1999). While little research has been done in this area, it appears that a sounds

level, frequency, movement parallax, and reflection play a role in judging distance.

There is an inverse relationship between sound level pressure and distance to the sound source such that as distance increases sound pressure decreases. This relationship suggests that the lower a sound's pressure is the greater the perceived distance of the sound source. However, research suggests that this is only the case when the sound is familiar to the listener (e.g. a person's voice). Frequency can also have an effect on the perception of distance. High frequencies are absorbed by the atmosphere at a greater rate than low frequencies causing sounds at a greater distance to appear muted (Middlebrooks & Green, 1991).

1.5 The Role of the Cortex in Localizing Sound

As early as 1958, researchers were able to demonstrate that participants with temporal lobe lesions had a greater difficulty localizing sounds than normal participants, particularly sounds originating in the contra-lateral field (Sanchez-Longo & Forster, 1958). While early studies failed to show dominance for either hemisphere in localizing sound (Sanchez-Longo & Forster, 1958; Shankweiler, 1961) more recent research suggest the right hemisphere may be dominant for localizing sound (Haeske-Dewick, Canavan, & Homberg, 1996; Braumgart et. al.,

1997; Weeks et. al., 1999; Kaiser, Lutzenberger, Preisl, Ackermann, & Birbaumer, 2000; Zatore & Penhune, 2001).

Haeske-Dewick, Canavan & Homberg (1996) investigated the role of the left and right hemispheres in auditory localization. They compared 10 right brain damaged, 10 left brain damaged and 10 control participants on a free field sound localization task. Participants were instructed to call out the number of the speaker they perceived a tone as coming from. Eight speakers were arranged at azimuths of -105° to 105°. A pattern of results was observed such that control subjects were most accurate at localizing sounds when the sound source was directly in front of them. They were slightly less accurate when the sounds were emitted form the speakers to their left and right. While overall less accurate than the control participants, the same pattern of results was observed for left hemisphere brain damaged participants. Right hemisphere brain damage participants, however, had difficulty localizing sounds from all directions suggesting the right hemisphere plays a particular role in forming a spatial frame of reference.

Baumgart et al. (1999) placed participants in an MRI and had them listen to stationary and moving sounds. The perception of movement was accomplished by varying the presentation of the sound in each ear. The fMRI data revealed that dependant upon whether the sound was moving or stationary

the right auditory cortex had significantly more activation than any other area of the auditory cortex. This study restricted the brain region of analysis to strictly the temporal lobes. However, it is not just the auditory cortex that is involved in auditory localizations, as the parietal lobes appear to play a particularly important role.

1.6 The Role of the Parietal Lobe in Localizing Sound

Visuospatial neglect typically occurs with right parietal and occipital lobe damage and results in an inattention to objects in the contra-lateral visual field (Lezak, 1995). Some visuospatial neglect patients respond to sounds (e.g. voices) that originated from their neglected side as if those sounds came from their unaffected side (Pavani, Ladavas, & Driver, 2002). This phenomenon is due, in part, to the strong connection between the visual and auditory senses in humans. For example, when watching a television program the sound coming from the speakers appears as though it is coming directly from the actor's mouth. There is no discrepancy between the two sensory stimuli as the brain takes the auditory information and the visual information and combines it together in such a way that the sound appears to be coming from a location it is not. This phenomenon is called visual capture (Lovelace & Anderson, 1993).

Soroker, Calamaro & Myslobodsky (1995) conducted an experiment with patients who had right hemisphere lesions with visuospatial neglect. When participants were presented with syllables played through a loud speaker on their neglected side they had difficulty identifying the syllables. When the same syllables were played again from a loud speaker positioned on the neglected side, but this time paired with a fictitious visual sound source in the unaffected side, performance improved. The authors attributed the effect of the fictitious visual sound source to the activation of an audiovisual map and used it as evidence of the coupling of the auditory and visual systems.

Another study showed that when visuospatial neglect patients were asked to point to the location of a sound source using their ipsilesional hand or by turning their heads toward the sound source they tended to incorrectly shift the sound source location toward their ipsilesional (right) side (Pinek, & Brouchon, 1992). However, an argument could be made that the corresponding auditory localization deficit is a function of an overall shift in all sensory modalities toward the ipsilesional (right) side rather than a true auditory localization deficit.

In order to distinguish between solely rightward shifts in spatial localization versus an overall impairment of auditory localization in visuospatial neglect patients, Pinek & Brouchon (1992) examined the ability of neglect patients to locate the vertical position of a sound source. Right brain-damaged

participants with and without visuospatial neglect were required to move a lever up or down in accordance with the vertical position of a target sound. Performance of the participants with visuospatial neglect was impaired compared to the participants without neglect. While the ability to localize auditory stimuli was impaired in neglect patients, it is important to note that other aspects of auditory processing were spared (e.g. the detection of the sound stimuli and perception of pitch). Given that all neglect participants had a portion of their lesions in the parietal lobe while the non-neglect participants did not suggested that the parietal lobe plays a crucial role in auditory localization.

Positron Emission Topography (PET) studies provide further evidence of the role of the parietal lobe in auditory localization (Bushara et al., 1999; Weeks et al., 1999: Weeks et al., 2000; Zatorre, Bouffard, Ahad, & Belin, 2002). Weeks et al. (1999) conducted a study in which they presented spectral and binaural cues of different sound locations through a set of headphones. In one condition participants were asked to make same/different discriminations about perceived sound locations and in another condition participants moved a joystick to indicate the perceived direction of the sound. Results revealed that the inferior parietal lobules were activated bilaterally during both the sound localization and feature discrimination tasks. However, the right inferior parietal lobule was significantly more active during the localization task.

Zatorre, Bouffard, Ahad, & Belin (2002) conducted a PET study in which they developed a way to present the sound stimuli within the PET scanner. This allowed listeners to localize sounds "with their own ears," as opposed to listening to simulated locations through a set of headphones. Data revealed significant activation of the right parietal lobe on two localization tasks.

Not all studies however suggest that the right parietal lobe is significantly more active than the left parietal lobe during localization tasks. In one PET study, Bushara et al. (1999) used synthesized sounds presented through headphones to "mimic sounds arriving from the free field." Subjects were instructed to move a joystick to indicate the perceived location of the sound. Data revealed bilateral activation of the superior and inferior parietal lobes.

Lewald, Foltys, & Topper (2002) used receptive transcranial magnetic stimulation to investigate the role of the posterior parietal cortex in the processing of auditory information. By generating high current pulses from a coil of wire which was placed above the scalp, magnetic fields were created that induced electrical fields. These electric field changes resulted in the uncoordinated stimulation of neurons, which interrupted normal brain activity. They discovered that with focal magnetic stimulation of both the left and right

posterior parietal cortices a systematic shift in sound lateralization of intraaural time differences occurred.

Previous research provides strong evidence of the cortex's role, particularly the parietal lobe, in auditory localization. Imaging studies which have focused on the role of the parietal lobe have primarily relied on positron emission topography to provide images of areas of brain activation. However, functional magnetic resonance imaging (fMRI) is an imaging technique that allows for a more detailed image of active cortical areas by providing higher spatial resolution (Wesinger et al., 2001; Jancke & Shah, 2002). The purpose of this study is to use fMRI to detect Blood Oxygen Level Dependant (BOLD) responses during an auditory localization task in hopes of providing a more detailed picture of parietal lobe activation. Based on past research, it is hypothesized that there will be significant activation of the parietal lobes during auditory localization tasks, with the right parietal lobe playing a more dominant role.

2. METHODS

2.1 Participants

Participants included nine adult volunteers with no history of neurological or audiological illness. Participants included seven females and two males who ranged in age from 20-31 years old. All participants were right handed. Due to limitations to the amount of time a person could comfortably tolerate the conditions of the MRI scanner, participants were divided in to two groups: a "Right-Side" group and a "Left-Side" group. One participant was a subject for both the left and right side conditions; therefore, there were a total of five participants in each condition. All participants provided informed consent and the study was approved by the Institutional Review Board of Drexel University.

2.2 Apparatus

The apparatus used for the sound sampling was a slightly modified version of the procedure used by Wightman, Kistler, Foster and Abel (1995). Two monaural miniature electret microphones configured as a stereo microphone (Radio Shack Catalog # 33-3028) were modified to fit into two small headphone frames that wrapped around the back of the external ear. The miniature microphone unit was placed in the auditory canal and the microphone cables ran

behind the head and down the back of the subject. The microphones were connected to a Shure Microphone Mixer to amplify the sound. The amplifier was connected to a Macintosh IBook laptop computer that contained the SoundEdit 16 (version 2, Macormedia) program. The SoundEdit 16 program was used to digitally record the sound samples.

2.3 Procedure

2.3.1 Sound Sampling

Participants, wearing the microphones, were placed on a rotating chair in the center of a room. A speaker was placed directly in front of the participant, ten feet away. In order to assure the participants head was oriented directly toward the speaker (0° azimuth) the participant wore headgear with an attached laser pointer. The participant was oriented on the chair so that the laser beam lined up with pre-measured and marked locations on the walls. The speaker then presented a 2500-hertz pure tone for one second. The microphone recorded the tone which was digitized and stored using the SoundEdit 16 program. The participant was then rotated on the stool 45°. The laser pointer attached to the headgear again assured that the participants head was correctly oriented 45° from the speaker. The speaker again presented a 2500-hertz pure tone for one second, which was recorded and stored by the SoundEdit 16 program. The

procedure was repeated until all sound samples were recorded. Participant in the Right-Side condition had sound recordings taken at 0°, 45°, 90°, 135°, and 180°. Participants in the Left-Side condition had sound recordings taken at 180°, 225°, 270°, 315°, and 0°.

2.3.2 Sound Verification

The SoundEdit 16 program was then used to present the sound recordings for a given angle through a set of headphones. The participant, sitting on the stool and oriented toward the 0° azimuth, was then asked to judge the approximate location of the sound by pointing. This step was done to verify that the participant perceived the recorded sound samples as coming from the correct location.

2.4 MRI Procedure

FMRI was performed using the Blood Oxygen Level Dependant (BOLD) contrast method. Magnetic resonance images were obtained using a standard clinical 1.5 Tesla Siemens Vision scanner (Siemens Gmbh., Enlargen, Germany). Brain scans were conducted with 26 contiguous no-gap 5-mm axial oblique image planes to cover the cerebrum. An imaginary line passing through the anterior-posterior commisures was used to position and align the slice planes.

This orientation was selected in order to assist a spatial transformation of obtained volumes into a standard anatomical space.

Anatomical references were acquired with high-resolution T_1-weighted images. The imaging parameters of the spin-echo sequence used to acquire the images were as follows: TR = 500 msec, TE = 14 msec, matrix size = 256^2 pixels, FOV = 22 X 22 cm^2, flip angle 90°, slice thickness = 5 mm; NEX = 1, and in-plane resolution = 0.86 x 0.86 mm^2. The T_2-weighted images were collected with an echo-planar imaging free induction decay (EPI-FID) single-shot pulse sequence. The positions of the T_2-weighted images were identical to those of the anatomical reference images. EPI-FID image parameters were as follows: TR = 4000 msec, TE = 54 msec, matrix size = 128^2 pixels, FOV = 22 X 22 cm^2, flip angle = 90°slice thickness = 5 mm, NEX = 1, band-width = 1470 Hz/pixel, and in-plane resolution = 1.72 X 1.72 mm^2. Shimming was performed for each data set as a way to reduce artificial fluctuations and inhomogeneties across images.

2.5 FMRI Paradigm

Participants were placed in the MRI scanner and instructed to get comfortable because once the testing began they would have to remain as still as possible. The participants were then instructed to close their eyes and that they would hear a series of tones followed by a pause. At the presentation of each

series of tones the participant was asked to determine the location of the sound. The subjects were instructed to think about the location and were asked not to make an overt verbal response. Active stimulus and rest conditions were presented using a conventional on-off boxcar design. Each series consisted of multiple periods of baseline at which point only the ambient noise of the MRI was heard, and periods of activation during which the tones were presented. The sequence consisted of 20 seconds of rest followed by 20 seconds of the activation condition. Scans of the whole brain were acquired every 4 seconds. The activation sequence was alternated six times, resulting in a set of 60 whole brain volumes (Fig. 1). A series for each of the five different sound sample locations (Right Side = 0°, 45°, 90°, 135°, 180°; Left Side = 180°, 225°, 270°, 315°, 0°) were presented to each of the subjects in a randomized fashion.

2.6 Analysis of fMRI Data

The analyses were performed with the software package SPM99 (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology, University College of London, UK), run under the Matlab® (The Mathworks, Inc., Natick, MA) software program. Region of interest (ROI) analyses were conducted using the WFU PickAtlas version 1.02 (Maldjian, Laurienti, Burdette,

& Kraft, 2003). This software allows for the generation of ROI masks based on the Talairach Daemon database.

2.6.1 Realignment, Normalization, and Smoothing

All collected images were converted from the Seiman's format in which they were initially stored into the ANALYZE (AnalyzeDirect, Inc., Lenexa, KY) format used by the SPM package. Next, a slice timing correction was performed which compensates for delays associated with acquisition time differences between slices during the imaging. This was done to adjust the MR signal's phase shift so that each volume has the signal values that would have been obtained had each slice been acquired first.

In the second step, a 3D automated image registration routine was applied to the volumes to realign them. The first volume of the first series was used as a spatial reference. Next all functional and anatomical volumes were transformed into the standard anatomical space (Talaraich & Tournoux, 1988) using the T_2 EPI template and the SPM normalization procedure (Ashburner & Friston, 1999). This procedure used a sinc interpolation algorithm which accounts for brain size and position. This step was used to correct for morphological differences between the template and the participants given brain volume. Next, all volumes underwent spatial smoothing by convolution with a Gaussian kernel to

increase the signal-to-noise ratio and account for residual intersession differences.

2.6.2 Activation Mapping

In order to determine the spatial extent of the recruited neurons and subsequently calculate the BOLD signal, SPM general linear model (GLM) procedures were used. This procedure resulted in the identification of the voxels associated with the auditory stimulation. By administering a series of voxel-based t-tests and creating statistical parametrical maps, a visual representation of the areas with statistically significant differences between the BOLD contrast responses elicited during the activation and rest conditions were created. Group analyses based on all subjects' data were then conducted for each sound location. Group analyses data are reported. Individual participants' data are presented in Appendix A.

3. RESULTS

3.1 Group BOLD responses during the localization tasks compared to rest

Compared to the resting state, the auditory localization task produced significant blood oxygenation changes in multiple areas of the cerebral hemispheres. Specifically, significant activation was observed in the areas of the parietal, temporal, and frontal lobes across all sound locations (Fig. 2). The pattern of temporal lobe activation revealed bilateral activation of the auditory cortex. Bilateral frontal lobe activation was also observed. However, it was not consistently observed to the same degree and in the same location of the frontal lobe.

The parietal lobes were isolated as a Region of Interest (ROI) using the PickAtlas program. This ROI analysis revealed consistent significant bilateral activation for all sound locations (Fig. 3 & Fig. 4). The right parietal lobe was not observed to be significantly more involved in the auditory localization tasks than the left parietal lobe (Table 1). For sound source locations 0° and 315° the right parietal lobe had more active voxel clusters. For sound source locations 45°, 180°, and 270° there were an equal number of active voxel clusters in the parietal lobes across the two hemispheres, and for sound source locations 90°, 135° and 225° the left parietal lobe had more active voxel clusters.

3.2 Tables and Figures

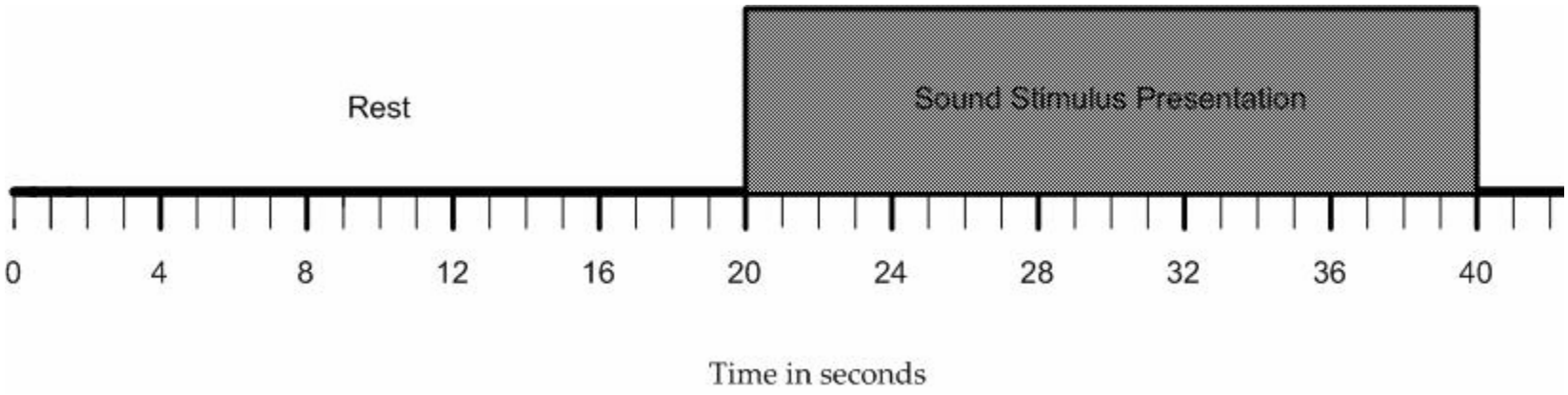

Figure 1. An example of the fMRI paradigm. The sequence consisted of 20 seconds of rest followed by 20 seconds of the activation condition. Scans of the whole brain were acquired every 4 seconds. The rest/activation sequence was alternated six times, resulting in a set of 60 whole brain volumes, which took a total of 240 seconds (4 minutes) to acquire.

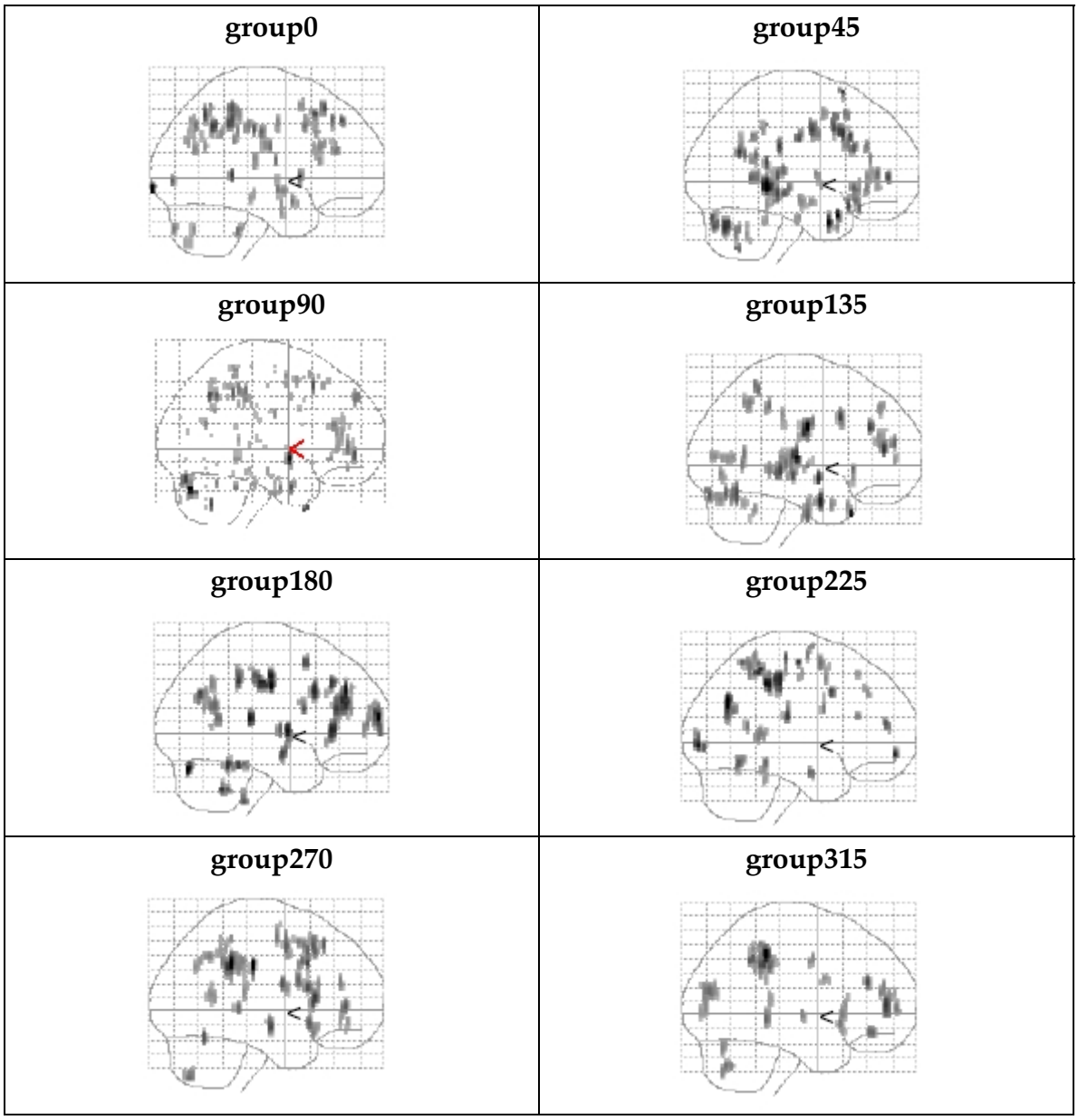

Fig. 2. Glass brain images of whole brain activation for each sound location based on group analyses. Neurological coordinates used.

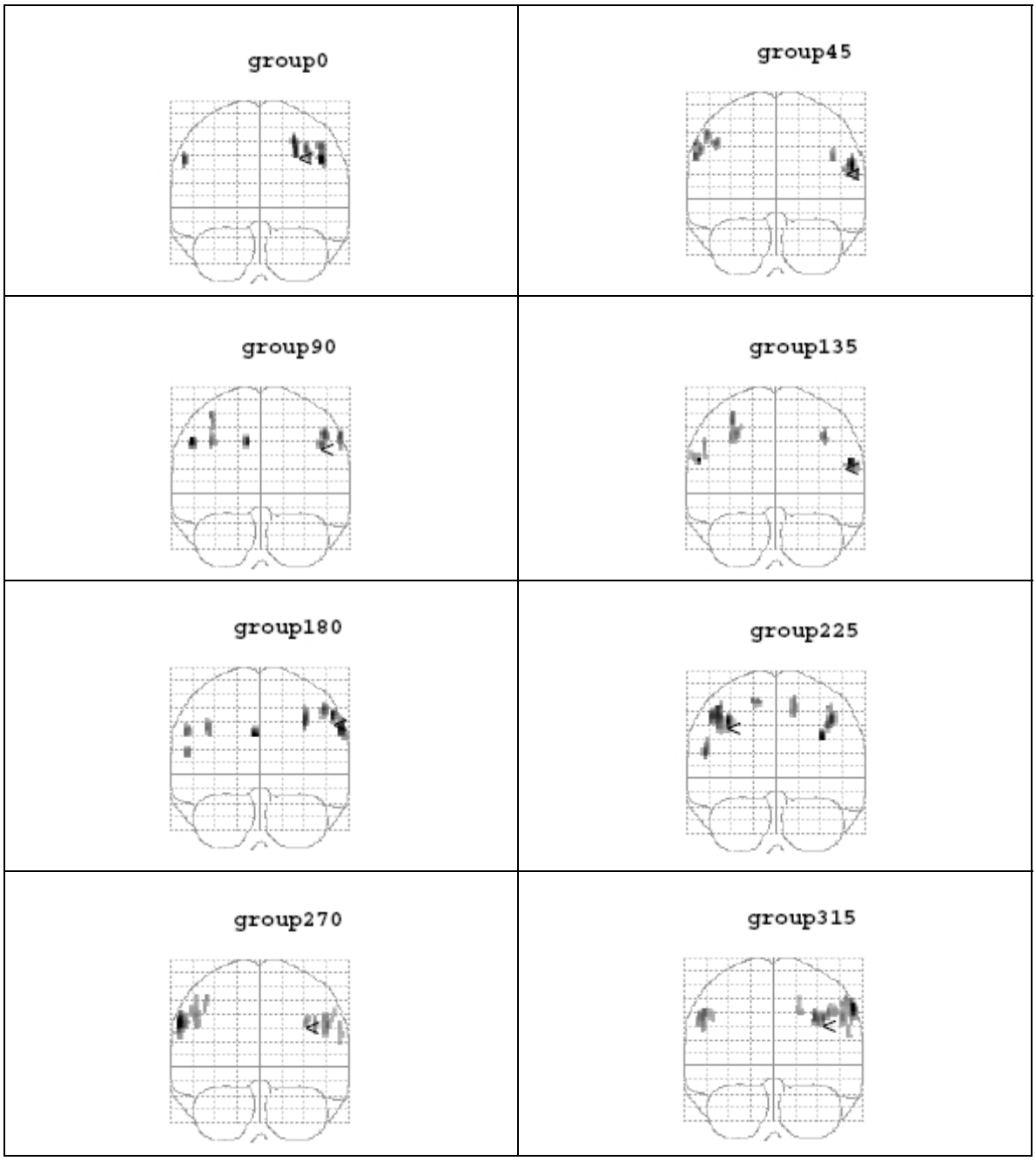

Fig. 3. ROI glass brain images of parietal lobe activation for each sound location based on group analyses. Images are in neurological coordinates.

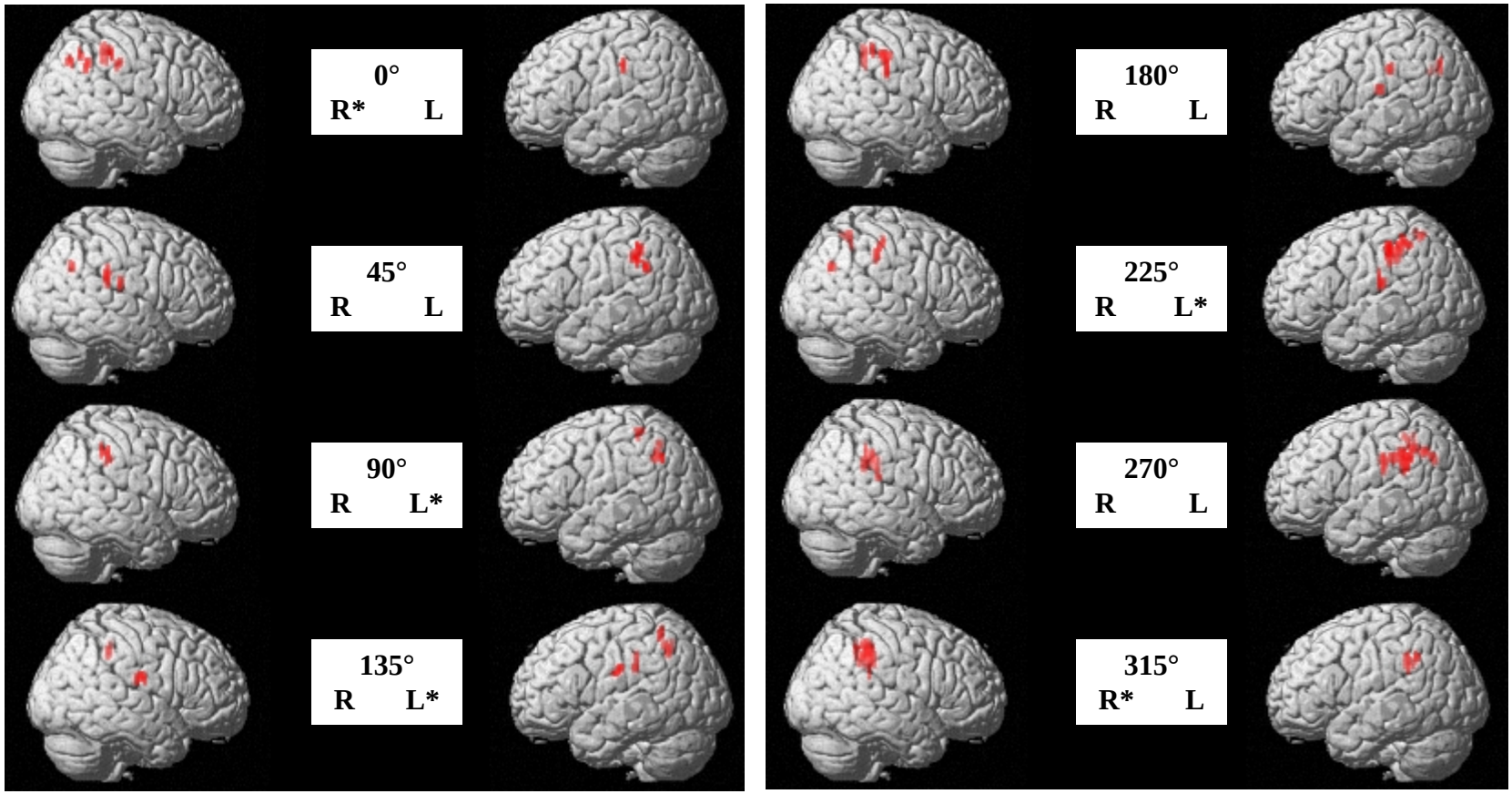

Fig. 4. ROI areas of activation of the right (R) and left (L) parietal lobes for each sound source location based on group analyses. The asterisk represents which parietal lobe had more active voxel clusters.

Table 1.
XYZ coordinates of active clusters for the right (R) and left (L) parietal lobe regions activated during the auditory localization task for each location. Significance levels and T-scores are provided.

Location	p-value	X, Y, Z Coordinates of Active Clusters	
		R Parietal Lobe (T-score)	L Parietal Lobe (T-score)
0°	.02	46, -34, 38 (3.09) 26, -40, 50 (2.88) 36, -50, 46 (2.63) 46, -34, 46 (2.61) 46, -28, 38 (2.56) 38, -55, 40 (2.53)	-58, -24, 38 (2.76)
45°	.03	58, -30, 26 (2.99) 62, -20, 20 (2.55) 44, -58, 32 (2.31)	-62, -50, 34 (2.55) -48, -38, 42 (2.45) -52, -42, 50 (2.43)
90°	.05	60, -32, 44 (2.26) 48, -38, 46 (2.24) 48, -32, 38 (2.13)	-52, -50, 40 (2.66) -10, -54, 40 (2.45) -38, -40, 60 (2.10) -38, -54, 40 (2.07)
135°	.01	56, -14, 24 (3.80) 38, -40, 44 (3.03)	-58, -12, 26 (4.08) -32, -48, 56 (3.15) -30, -54, 46 (2.91) -54, -30, 38 (2.68)
180°	.01	54, -28, 46 (3.60) 60, -26, 36 (3.54) 34, -44, 40 (3.41) 48, -40, 50 (3.27	-4, -58, 30 (3.81) -56, -34, 24 (2.99) -40, -54, 36 (2.92) -54, -16, 18 (2.87)

Table 1 (continued)

225°	.02	36, -66, 30 (3.85)	-36, -38, 44 (3.62)
		42, -28, 44 (3.38)	-44, -28, 48 (3.43)
		14, -50, 56 (2.73)	-44, -42, 54 (3.31)
			-54, -22, 20 (3.18)
			-18, -56, 60 (2.88)
270°	.01	50, -40, 32 (3.41)	-62, -24, 34 (4.73)
		42, -34, 32 (3.04)	-60, -40, 34 (4.68)
		36, -34, 34 (3.03)	-48, -56, 40 (3.11)
		50, -34, 38 (2.96)	-40, -40, 52 (2.90)
		60, -30, 30 (2.63)	-48, -48, 44 (2.74)
315°	.02	60, -38, 44 (4.38)	-52, -50, 40 (3.18)
		32, -40, 38 (3.44)	
		52, -34, 38 (2.95)	
		20, -46, 40 (2.58)	

4. DISCUSSION

The present study revealed a combination of parietal, frontal, and temporal lobe activation that occurs during auditory localization. The presence of temporal and frontal lobe activation is consistent with previous research. Bushara et al. (1999) conducted a PET study that used synthesized sounds to mimic free field locations. They reported areas of activation which included the posterior parietal lobule, middle temporal and lateral prefrontal cortices. They took these findings to support the notion that, similar to the organization of the visual system, the auditory system has a hierarchical organization. Part of this organization includes areas of the frontal and parietal lobes which are specialized for processing spatial information.

Given the nature of the task in the present study, listening to sounds, it is not surprising that activity in the temporal lobes was observed as the primary auditory cortex lies in this region. Neuropsysiological studies from several species have shown that the primary auditory cortex is sensitive to intraaural cues for azimuth position (Zatorre & Penhune, 2001).

Frontal lobe activation may be explained by the high attentional demands of the task. Subjects were instructed to try to determine the location the sound appeared to be coming from while in the scanner. This required selectively attending to the sound stimuli. Spatial selective attention has been linked to the

frontoparietal regions (Bushara et al., 1999). Also, the ambient scanner noise may have been competing with the experimental stimuli. As a result, subjects may have been actively inhibiting the ambient scanner noise in order to better attend to the sound stimuli, which would have resulted in frontal lobe activation. In addition to the posterior parietal and middle temporal cortices, working memory of audiospatial information has also been linked to areas in the superior, middle, and inferior frontal gyri (Martinkauppi, Rama, Aronen, Korvenoja, & Carlson, 2000)

Inconsistent with previous studies (e.g. Pinek, & Brouchon, 1992; Weeks et al., 1999; Zattore, et al., 2002) a preferential role of the right parietal lobe was not consistently observed in this study. Only two of the eight sound source locations (0° and 315°) had more active clusters in the right parietal lobe than the left. In three cases (45°, 180°, & 270°) there were an equal number of active clusters across the hemispheres and in the other three cases (90°, 135°, & 225°) the left parietal lobe had more active clusters than the right parietal lobe. Of note is the fact that the previous studies that have shown greater right parietal lobe activation during localization tasks have not distinguished areas of activation across different locations. Analyses in these studies involve localization in general and disregard potential differences in localization for different sound source positions. Based on the present results, it is possible that the left parietal

lobe plays more of a role in localization for specific sound locations than the right parietal lobe and vice versa. This may partially explain why greater right parietal lobe activation was not consistently observed in the present study. In addition, the possibility that activations within the right parietal lobe may have been too subtle to be detected by MRI should be considered.

One confound to this study is that the ambient scanner noise may have affected the subjects' ability to accurately localize the sound stimuli. The sound stimuli presented to the subjects while in the scanner was 2500 Hz, arbitrarily chosen because it falls within the middle range of the human voice. The frequency of the ambient scanner noise, however, was never measured. It is possible that the frequency of the scanner noise was similar to the sound stimuli played to the subjects through the headphones. If this was the case, it could have affected subjects' ability to accurately localize the sound stimuli presented through the headphones.

One way to help control for the effects of the ambient scanner noise, as put forth by Jancke & Shah (2002), would be to adjust the timing of the sound stimuli presentation. The noise of the MRI scanner, mostly a result of moving gradient coils, produces a BOLD response, which can mask the BOLD response associated with the experimental stimuli. Jancke & Shah (2002) controlled for this effect by adjusting the presentation of the experimental stimuli such that the experimental

stimuli were presented during the interscan gap. As a result, when scanning started the BOLD responses produced by the experimental stimuli had already been elicited and were at their peak. Therefore, the initial scanning images capture the BOLD responses associated with the experimental stimuli, as the BOLD responses associated with the ambient scanner noise have not yet reached their peak.

Participants in this study were instructed not to respond while in the scanner, but only think about the perceived location of the sound stimuli. It was decided not to have the subjects respond while in the scanner because they had already verified, through the sound stimulus sampling procedure, that they could accurately localize the direction of the sound stimuli. However, by choosing not to have them verify the sound source location while in the scanner, there is no data available to test the hypothesis that the ambient scanner noise may have affected the perceived sound stimulus location.

Perhaps by increasing the spatial demands of the auditory localization tasks greater right parietal lobe activation would be elicited. The majority of the auditory localization studies involve the presentation of pure tones as auditory stimuli. An interesting twist on future studies of auditory localization could include the presentation of more "real world" complex sounds, such as speech sounds, as a way to determine the pattern of activation for complex versus

simple sounds. Another way to increase the spatial demands of the task would be to present multiple sound locations within the same MRI series. This method could help control for any effects habituation may have on the level of activation.

Another topic to consider when discussing the present results is what effect, if any, lying down in the scanner had on the perceived direction of the sound source. When the sound samples were recorded, the participants were sitting upright on a stool. However, when the MRI images were obtained the participants were in the supine position. While a literature review failed to find any studies pertaining to this topic in particular, a study by Lewald & Kamath (2002) examines the effect of whole body tilt on sound lateralization. They had participants strapped in to a chair in a "cabin" that rotated 45° and 90° to the right and left. They discovered that when the body was tilted the auditory median plane of the head was shifted to the upward facing ear, which indicated a shift of the auditory percept to the downward facing ear. This is an interesting area of further research given the number of localization studies that now involve Neuroimaging, which typically requires participants to be in the supine position.

This study and recent PET studies have provided further evidence of the role of the parietal lobe in auditory localization. However, this study does not provide support for the hypothesis that the right parietal lobe is more active than

the left parietal lobe during auditory localization tasks. Further fMRI research that helps control for the above mentioned confounds would help clarify the role of the parietal lobes in auditory localization.

List of References

Ashburn, J, & Friston, KJ. (1999). Nonlineral spatial normalization using basis functions. Human Brain Mapping, 7, 254-266.

Baumgart, F, Gaschler-Markefski, B, Woldorff, MG, Heinze, H-J, Scheich, H. (1999). A movement-sensitive area in the auditory cortex. Nature, 400, 724-726.

Bushara, KO, Weeks, RA, Ishii, K, Catalan, M-J, Tian, B, Rauschecker, JP, & Hallet, M. (1999). Modality-specific frontal and parietal areas for auditory and visual spatial localization in humans. Nature Neuroscience, 2, 759-766.

Cranford, J, Ravizza, R, Diamond, IT, & Whitfield, IC. (1971). Unilateral ablation of the auditory cortex in the cat impaires complex sound localization. Science, 172, 286-288.

Durlach, N & Colburn, H (1978). Binaural Phenomena. In: Carterette E.C., Friedman, M.P. (eds) Handbook of perception: Vol IV – Hearing (pp. 365-466). New York: Academic Press.

Gardner, MB & Gardner, RS (1973). Problem of localization in the medial plane: Effect of pinnae cavity occlusion. Journal of the Acoustical Society of America, 53, 400-408.

Goldstein, EB (2002). Sensation and perception. Pacific grove, CA: Wadsworth.

Haeske-Dewick, H, Canavan, AGM & Homberg, V. (1996). Sound localization in egocentric space following hemispheric lesions. Neuropsychologia, 34, 937-942.

Heffner, H, & Masterson, B. (1975). Contribution of the auditory cortex to sound localization in the monkey (Macaca mulatta). Journal of Neurophysiology, 38, 1340-1358.

Jancke, L, & Shah, NJ. (2002). Does dichotic listening probe temporal lobe functions? Neurology, 58, 736-743.

King, AJ, Schnupp, JWH, & Doubell, TP. (2001). The shape of ears to come: dynamic coding of auditory space. TRENDS in Cognitive Science, 5, 261-270.

Knudsen, EL, & Konishi, M. (1978). A neural map of auditory space in the owl. Science, 200, 795-797.

Lewald, J, Foltys, H., Topper, R. (2002). Role of the posterior parietal cortex in spatial hearing. The Journal of Neuroscience, 22, RC207, 1-5.

Lezak, MD. (1995). Neuropsychological Assessment. New York: Oxford University Press

Lovelace, EA, & Anderson, DM. (1993). The role of vision in sound localization. Perceptual and motor Skills, 77, 843-850.

Maldjian, JA, Laurienti, PJ, Burdette, JB, Kraft, RA. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas based interrogation of fMRI data sets. NeuroImage, 19, 1233-1239.

Martin, J (1996). Neuroanatomy text and atlas (2nd ed.). Stamford, CT: Appleton & Lange.

Martinkauppi, S., Rama, P, Aronen, HJ, Korvenoja, A, & Carlson, S. (2000). Working memory of Auditory localization. Cerberal Cortex, 10, 889-898.

Middlebrooks, JC (1997). Spectral shape cues for sound localization. In RH Glickel & TR Anderson (Eds.) Hillsdale, NJ: Earlbaum.

Middlebrooks, JC, & Green, DM (1991). Sound localization by human listeners. Annual review of Psychology, 42, 135-159.

Mohamed, FB, Pinus, AB, Faro, SH, Patel, D, & Tracy, J (2002). BOLD fMRI of the visual cortex: quantative responses measured with a graded stimulus at 1.5 tesla. Journal of Magnetic Resonance Imaging, 16, 128-136.

Moore, B (1992). An introduction to the psychology of hearing. New York: Academic press.

Morrell, F. (1972). Visual system's view of acoustic space. Nature, 238, 44-46.

Pavani, F, Ladavas, E, & Driver, J. (2002). Selective deficit of auditory localization in patients with visuospatial neglect. Neuropsychologia, 40, 291-301.

Pinek, B, & Brouchon, M. (1992). Head turning versus manual pointing to auditory targets in normal subjects and in subjects with right parietal damage. Brain and Cognition, 18, 1-11.

Pinek, B, Duhamel, J-R, Cave, C, & Brouchon, M (1989). Audio-spatial deficits in humans: differential effects associated with left versus right hemisphere parietal damage. Cortex, 25, 175-186.

Rosenblatt, CE (1999). Auditory localization in visual neglect patients. Dissertation Abstracts International: Section B: the Sciences and Engineering, 59 (9-b), 5155. (University Microfilms).

Sanchez-Longo, LP & Forster, FM (1958). Clinical significance of impairment of sound localization. Neurology, 8, 119-125.

Shankweiler, DP. (1961). Performance of brain damages patients on two tests of sound localization. Journal of Comparative Physiology and Psychology, 54, 375-381.

Simmons, P, & Young, D. (1999). Nerve Cells and Animal Behavior (2nd ed.). New York: Cambridge University Press.

Soroker, N, Calamaro, N & Myslobodsky, MS (1996). Ventriloquist effect reinstates responsiveness to auditory stimuli in the "ignored" space in patients with hemispatial neglect. Journal of Clinical & Experimental Neuropsychology, 17, 243-255.

Talaraich, J & Tournoux, P (1988). Co-planar stereotaxic atlas of the human brain. New York: Georg Thieme Verlag.

Weeks, R, Horwitz, B, Aziz-Sultan, A, Tian, B, Wessinger, M, Cohen, L, Hallett, M, & Rauschecker, J.P (2000) A positron emission tomographic study of auditory localization in the congenitally blind. The Journal of Neuroscience, 20, 2664-2672.

Weeks, R, Aziz-Sudan, A, Bushara, K, Tian, B, Wessinger, C, Dang, N, Rauschecker, J, Hallett, M (1999). A PET study of human auditory spatial processing. Neuroscience Letters, 262, 155-158.

Wessinger, CM, Buonocore, MH, Kussmaul, MH, & Mangun, GR. (1997). Tonotopy in human auditory cortex examined with functional magnetic resonance imaging. Human Brain Mapping, 5, 18-25.

Wightman, F.L. Kistler, D. J., Foster, S. J. and Abel, J. (1995). A comparison of head related transfer functions measured deep in the ear canal and at the ear canal entrance. Presented the Annual Meeting of the Association for Research in Otolanyngology.

Wrightman, FL & Kistler, DJ (1993). Sound Localization. In WA Yost, AN Popper, & RR Fay (Eds.), Human psychophysicis (pp. 155-192). New York: Springer.

Zatorre, RJ & Penhune, VB. (2001). Spatial localization after excision of the human auditory cortex. The Journal of Neuroscience, 21, 6321-6328.

Zatorre, RJ, Bouffard, M, Ahad, P, & Belin, P. (2002). Where is "where" in the human auditory cortex? Nature Neuroscience, 5, 905-909.

Appendix A. Individual Subjects' data for each sound location

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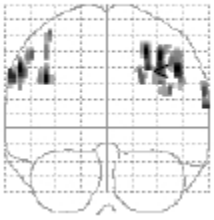
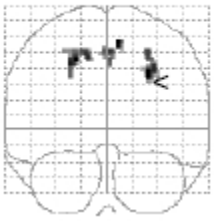
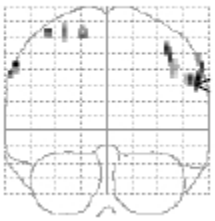
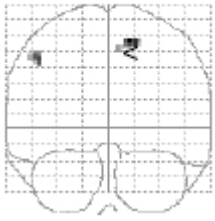
am0 
an0 
b0 
c0 

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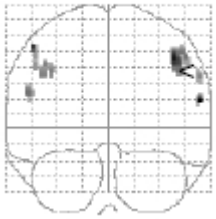

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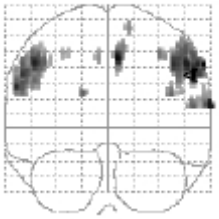

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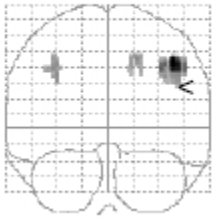

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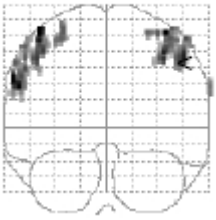

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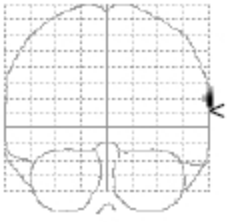

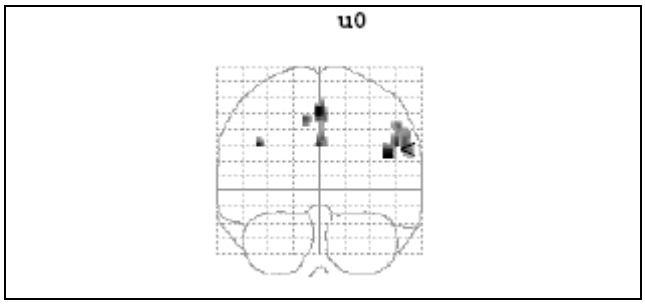
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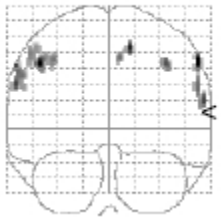
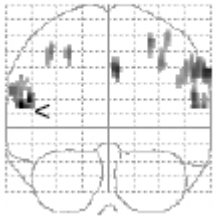
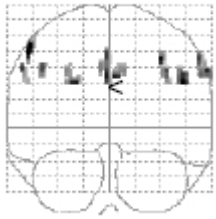
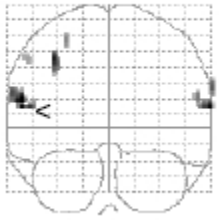
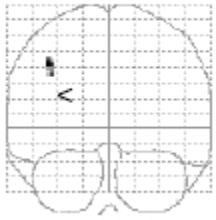
c45 
j45 
m45 
sm45 
sv45 

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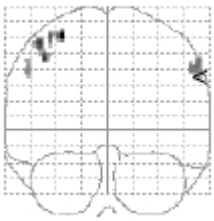
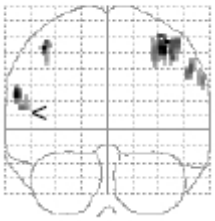
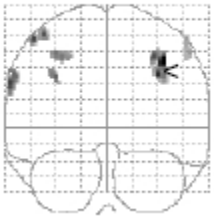
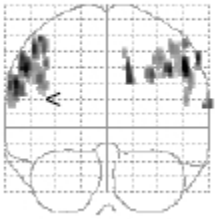
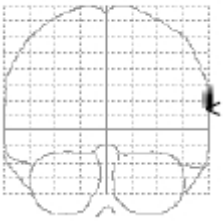
c90 
j90 
m90 
sm90 
sv90 

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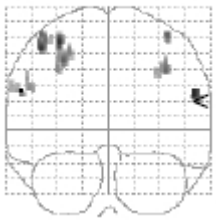
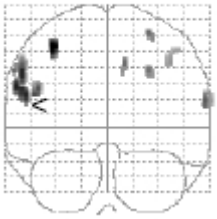
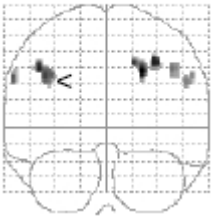
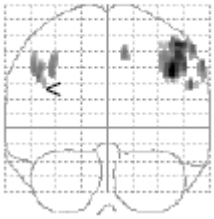
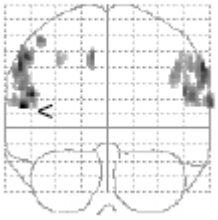
c135 
j135 
m135 
sm135 
sv135 

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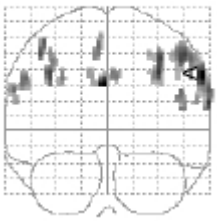
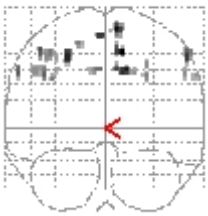
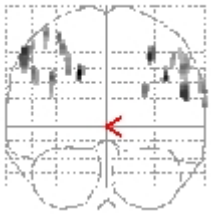
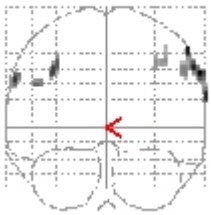
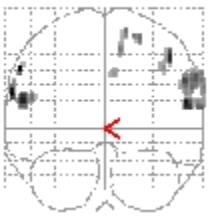
am180 
an180 
b180 
c180 
j180 

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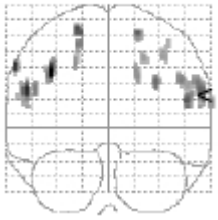
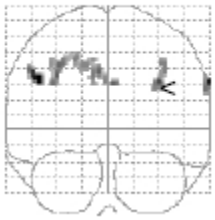
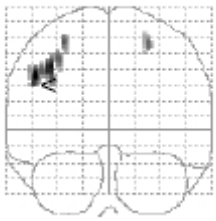
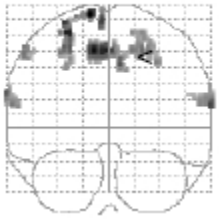
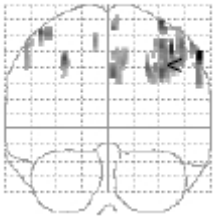
jl180 
m180 
sm180 
sv180 
u180 

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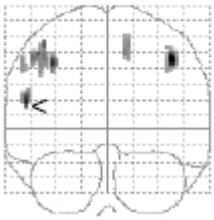
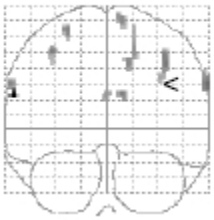
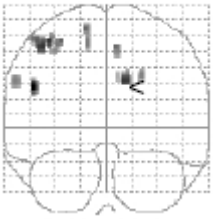
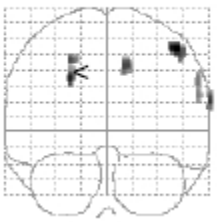
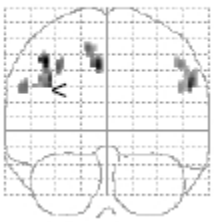
am225 
an225 
b225 
j1225 
u225 

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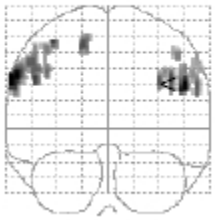
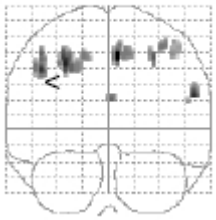
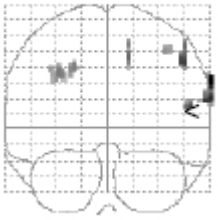
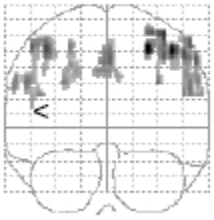
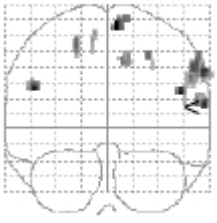
am270 
an270 
b270 
j1270 
u270 

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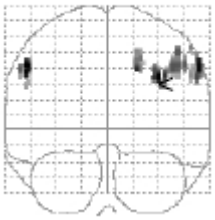
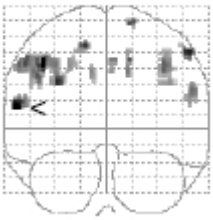
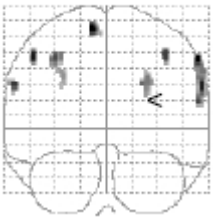
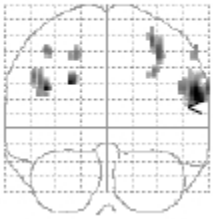
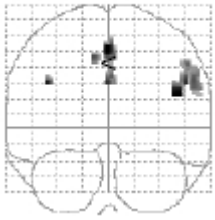
am315 
an315 
b315 
j1315 
u315 

Vita

Jessica Marie Matthes was born and raised in Willimantic, CT. She attended the University of North Carolina at Wilmington where she earned a B.S. in Marine Biology and a B.A. and M.A. in Psychology. She currently attends Drexel University where she will soon earn a Ph.D. in Clinical Psychology with a specialization in Neuropsychology. She will soon complete her Neuropsychology Specialty Track Pre-Doctoral Internship at the Southern Arizona VA Healthcare System in Tucson, AZ. She plans to receive Post-Doctoral Training in Neuropsychology at Barrow Neurological Institute in Phoenix, AZ.